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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,023	03/23/2004	Shirlynn Chen	9/279	2248

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/807,023	CHEN ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 March 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and the species of formulation 3, in the reply filed on December 1, 2005 is acknowledged. The traversal is on the ground(s) that the compounds of formula (I) are closely related and are a proper Markush group, sharing a common structural core, and that all of the compositions are closely related, requiring the same generic elements.

This is not found persuasive because the composition of claim 1 embraces a myriad of compositions, each requiring a different search, and thus it would be an undue burden to search the myriad of compositions which are embraced by the claims and the methods of using said compositions.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's elected species has been found to be free of the prior art, however no claim(s) is/are drawn specifically to the elected species. The examiner extended the search to embrace the generic structure of formula (I).

Specification

The disclosure is objected to because of the following informalities:

The use of the trademark(s), e.g., Captex 355, Kollidon 90 PF, Cremophor EL [please note, this list is exemplary and does not identify all trademarks in the specification], has/have been noted in this application. A trademark should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant should capitalize each letter of the word or include a proper trademark symbol, such as ™ or ® following the word. Further, language such as "the product X (a descriptive name) commonly known as Y (trademark)" is impermissible, since such language does not bring out the fact that the latter is a trademark. Language such as "the product X (a descriptive name) sold under the trademark Y" is permissible. See MPEP § 608.01 (v).

The reference to Chen as US Application 10/357,919, page 4, line 22) should be updated to reflect the issued patent number 6,828,301 B2.

The description of the drawings (page 7) does not adequately describe the information presented in the figures, nor does the figures provide a 'key' to the compounds being tested or what is being described beyond two formulations having different levels of impurities of different degradation products.

Appropriate correction is required.

Drawings

The drawings are objected to because there is no legend or key, in the figure or in the specification (Brief Description of the Drawings) to describe what is being depicted in the figure. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be

labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

The objection may be overcome by amendment to the specification, as presented *supra* (*see Specification*).

Claim Objections

Claim 1 is objected to for having an additional period after the structure of formula (I). MPEP § 804.01(m) states that, "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See *Fressola v. Manbeck*, 36 USPQ2d 1211 (D.D.C. 1995)."

Claim 7 is objected to because the Markush group does not have 'and' or 'or' between the last two recited species.

Claim 24 is objected to because of the following informalities: The trademark Cremophor EL is in parenthesis, and while exemplary of the surfactant, requires proper identification as a trademark. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 recite trademark compounds- Capmul® MCM and Captex® 355. It is unclear what is being claimed, as trademarks do not define static compositions, as they are capable of being changed or reformulated, and thus the claim is indefinite. Further, in looking at the Product sheet from ABITEC for Captex® 355 (see enclosed) the "typical fatty acid distribution by GLC" is 6 % max 6:0 caproic acid; 50-75% 8:0 caprylic acid; 22-45% 10:0 capric acid; and 4% max 12:0 lauric acid, which does not clearly define what the composition comprises.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 8-22, 26 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by CHEN (US Patent 6,828,301 B2) as evidenced by PATEL (US 2001/0024658 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. § 102(e).

This rejection under 35 U.S.C. § 102(e) might be overcome either by:
(1) a showing under 37 CFR § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or
(2) by an appropriate showing under 37 CFR § 1.131.

The rejection set forth is based upon the interpretation that the amine and base may be the same compound.

Patel is relied upon for the beneficial teaching that tris(hydroxymethyl)aminomethane (tromethamine) is a pharmaceutically acceptable base, as well as an amine. Tromethamine meets the limitations of being both the amine and the base, as Patel teaches it to be a base (paragraph [0098]).

The instant claims are drawn generally to pharmaceutical compositions comprising compounds of formula (I); pharmaceutically acceptable amine(s), base(s) and oil(s); and optionally pharmaceutically acceptable hydrophilic solvent(s), polymer(s) and surfactant(s).

Chen teaches pharmaceutical compositions comprising compounds of formula (I); pharmaceutically acceptable amine(s) and oil(s); and optionally pharmaceutically acceptable hydrophilic solvent(s), polymer(s) and surfactant(s) (claims 1-30).

Specifically, Chen teaches a composition comprising (all by % weight): about 10-20% of a compound of formula (I); about 0.1-5% tromethamine; about 20-70% mono- or diglycerides of caprylic fatty acid or capric fatty acid, or mixtures thereof; about 10-30% propylene glycol, ethanol and optionally water; about 1-20% PEG or PVP; and about 20-50% V_e TPGS or polyoxyl-35 castor oil (claim 28).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1-27 are rejected under 35 U.S.C. § 103(a) as being obvious over CHEN in view of PATEL, as applied to claims 1-6, 8-22, 26 and 27, *supra*, and in further view of TSANTRIZOS (US Patent 6,608,027 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e).

This rejection under 35 U.S.C. § 103(a) might be overcome by:

(1) a showing under 37 CFR § 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another";

(2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR § 1.131;

(3) an oath or declaration under 37 CFR § 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR § 1.321(c); or

(4) a showing that the reference is disqualified under 35 U.S.C. § 103(c) as prior art in a rejection under 35 U.S.C. § 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant claims and the teachings of Chen are presented *supra*.

Chen further teaches that "If desired, the compositions according to the present invention may further include conventional pharmaceutical additives as is necessary or desirable to obtain a suitable formulation, such as antioxidants, lubricants, disintegrants, preservatives, buffers, stabilizers, ...Additional additives that may be useful in the compositions of the invention are disclosed in Tsantrizos, et al." (column 17, lines 30-38). [It is noted that Tsantrizos cited by Chen is now issued US Patent 6,608,027 B1, *supra*].

The claims of Chen generally correspond to the instant claims as shown in the following table:

Application Claim #	1	2	3	4	5	8	9	10	11
Chen Claim #	1	2	3	4	5	27	7	8	9

Application Claim #	12	13	14	15	16	17	18	19	20
Chen Claim #	10	11	12	13	14	15	1	22	23

Application Claim #	21	22	23	24	25	26	27
Chen Claim #	24	26	27	28	31,32	29	30

Tsantrizos teaches compounds that are embodied by instant formula (I), including the species #822 (e.g.- Table 8 compounds, columns 129-135).

Tsantrizos teaches that the compositions, "may contain any conventional non-toxic pharmaceutically acceptable carries or auxiliary agents such as adjuvants or vehicles. In some cases, the pH of the formulation may be adjusted with pharmaceutically acceptable acids, bases or buffers to enhance the stability of the formulated compound or its delivery form." (column 12, lines 26-33).

Tsantrizos teaches that magnesium stearate is a lubricating agent that is "typically added to oral dosage forms" (column 12, lines 54-55).

Patel teaches that acids or bases are incorporated into compositions, "to facilitate processing, to enhance stability, or for other reasons. Examples of pharmaceutically acceptable bases include... ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, magnesium hydroxide, magnesium aluminum silicate, ..., ethanolamine, ethylenediamine, triethanolamine, triethylamine, ... [tromethamine], and the like. Also suitable are bases that are salts of a pharmaceutically acceptable acid, such as ...fatty acids..." (paragraph [0098]). Stearic acid as the magnesium salt is magnesium stearate, which is the salt of a fatty acid, and thus a base.

The difference between that which is instantly claimed, and that which is taught by the prior art, is that while Chen teaches the composition, Chen does not teach the specifically recited bases being used, or the combinations with the specifically recited concentration ranges.

It would have been obvious at the time of the invention to have made the composition of Chen with the addition of magnesium stearate or any other base, including ammonium hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, magnesium hydroxide, as the base in order to increase fluidity, facilitate processing or to enhance the stability of the composition.

One would have been motivated to have used sodium hydroxide, or any base, in the composition, as Chen teaches that the composition can "further include conventional pharmaceutical additives as is necessary or desirable to obtain a suitable formulation, such as

antioxidants, lubricants, disintegrants, preservatives, buffers [or] stabilizers", in order to increase the fluidity of the composition or enhance the stability of the composition.

One would have had a reasonable expectation for success in making the composition with any base, including sodium hydroxide, as Chen teaches that any antioxidants, lubricants, disintegrants, preservatives, buffers, stabilizers can be added to obtain a 'suitable formulation', Tsantrizos teaches that any base can be added to adjust the pH and increase the stability of the formulated compound, and because Patel teaches that any pharmaceutically acceptable base can be incorporated to increase stability and facilitate processing of a compound.

Further, with regards to the specific ranges claimed for the base and the compositions, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. concentrations or ratios), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8-22, 26 and 27 are rejected on the ground of nonstatutory double patenting over claims 1-32 of CHEN (US Patent 6,828,301 B2) in view of PATEL (US 2001/0024658 A1) since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows:

The rejection set forth is based upon the interpretation that the amine and base may be the same compound.

Patel is relied upon for the beneficial teaching that tris(hydroxymethyl)aminomethane (tromethamine) is a pharmaceutically acceptable base, as well as an amine. Tromethamine meets

the limitations of being both the amine and the base, as Patel teaches it to be a base (paragraph [0098]).

The instant claims are drawn generally to pharmaceutical compositions comprising compounds of formula (I); pharmaceutically acceptable amine(s), base(s) and oil(s); and optionally pharmaceutically acceptable hydrophilic solvent(s), polymer(s) and surfactant(s).

Chen teaches pharmaceutical compositions comprising compounds of formula (I); pharmaceutically acceptable amine(s) and oil(s); and optionally pharmaceutically acceptable hydrophilic solvent(s), polymer(s) and surfactant(s) (claims 1-30).

Specifically, Chen teaches a composition comprising (all by % weight): about 10-20% of a compound of formula (I); about 0.1-5% tromethamine; about 20-70% mono- or diglycerides of caprylic fatty acid or capric fatty acid, or mixtures thereof; about 10-30% propylene glycol, ethanol and optionally water; about 1-20% PEG or PVP; and about 20-50% V_e TPGS or polyoxyl-35 castor oil (claim 28).

Claims 1-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-30 of CHEN (US Patent 6,828,301 B2) in view of PATEL (US 2001/0024658 A1) and in further view of TSANTRIZOS (US Patent 6,608,027 B1).

The instant claims and teachings of Chen, Patel and Tsantrizos are presented *supra*. The difference between that which is instantly claimed, and that which is taught by the prior art, is that while Chen teaches the composition, Chen does not teach the specifically recited bases being used, or the combinations with the specifically recited concentration ranges.

It would have been obvious at the time of the invention to have made the composition of Chen with the addition of magnesium stearate or any other base, including ammonium

hydroxide, potassium hydroxide, sodium hydroxide, sodium hydrogen carbonate, aluminum hydroxide, calcium carbonate, magnesium hydroxide, as the base in order to increase fluidity, facilitate processing or to enhance the stability of the composition.

One would have been motivated to have used sodium hydroxide, or any base, in the composition, in order to increase the fluidity of the composition or enhance the stability of the composition.

One would have had a reasonable expectation for success in making the composition with any base, including sodium hydroxide, as the composition of Chen allows for additional elements which are not specifically recited, Tsantrizos teaches that any base can be added to adjust the pH and increase the stability of the formulated compound, and because Patel teaches that any pharmaceutically acceptable base can be incorporated to increase stability and facilitate processing of a compound.

Further, with regards to the specific ranges claimed for the base and the compositions, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. concentrations or ratios), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). *See* MPEP § 2145.05).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

NO CLAIMS ARE ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Andrew D. Kosar, Ph.D.
Art Unit 1654

ANISH GUPTA
PRIMARY EXAMINER